

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

KEITH W NASH & CO.
90-92 Regent Street
Cambridge CB2 1DP
ROYAUME-UNI

Date of mailing (day/month/year) 04 October 2000 (04.10.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference ML/C155.1/0	
International application No. PCT/GB99/01650	International filing date (day/month/year) 26 May 1999 (26.05.99)

1. The following indications appeared on record concerning:	
<input checked="" type="checkbox"/> the applicant	<input checked="" type="checkbox"/> the inventor <input type="checkbox"/> the agent <input type="checkbox"/> the common representative
Name and Address LAMBERT, Peter, Anthony 10 Dunton Close Sutton Coldfield Birmingham B75 5QD United Kingdom	State of Nationality GB
	State of Residence GB
	Telephone No.
	Facsimile No.
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:	
<input type="checkbox"/> the person <input type="checkbox"/> the name <input checked="" type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence	
Name and Address LAMBERT, Peter, Anthony 125 Walsall Road Sutton Coldfield West Midlands B74 4NR United Kingdom	State of Nationality GB
	State of Residence GB
	Telephone No.
	Facsimile No.
3. Further observations, if necessary:	
4. A copy of this notification has been sent to:	
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Jocelyne Rey-Millet Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
 United States Patent and Trademark
 Office
 Box PCT
 Washington, D.C.20231
 ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year)

15 December 1999 (15.12.99)

International application No.

PCT/GB99/01650

Applicant's or agent's file reference

ML/C155.1/0

International filing date (day/month/year)

26 May 1999 (26.05.99)

Priority date (day/month/year)

28 May 1998 (28.05.98)

Applicant

LAMBERT, Peter, Anthony et al

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

25 November 1999 (25.11.99)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Juan Cruz

Telephone No.: (41-22) 338.83.38

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference ML/C155.1/0	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 99/01650	International filing date (day/month/year) 26/05/1999	(Earliest) Priority Date (day/month/year) 28/05/1998
Applicant OXOID LIMITED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

ANTIBACTERIAL DIASCCHARIDE DERIVATIVES

5. With regard to the **abstract**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

2

☒ as suggested by the applicant.

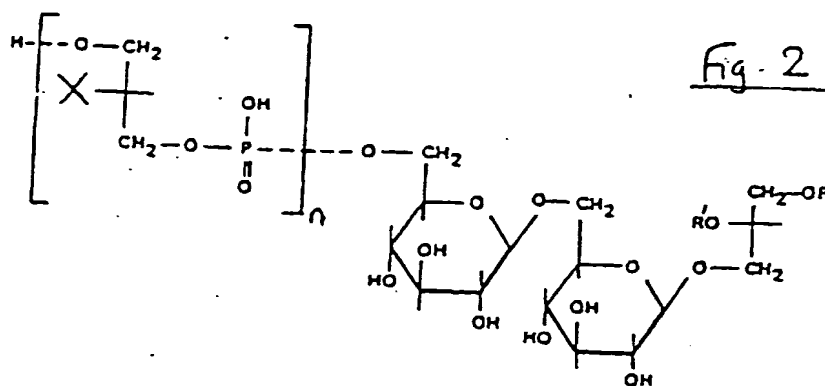
☐ None of the figures.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

Disclosed is an isolated compound having the structure shown in Figure 2, wherein n is an integer between 3 and 10 (inclusive) and X may be H, OH, alkyl, aryl, amyl, or an amino acid residue (optionally substituted) or a sugar residue (optionally substituted), and wherein R and R' are hydrophobic hydrocarbon or fatty acid chains (R may be the same as R' or different), a method of preparing compositions comprising the compound, and a diagnostic method comprising use of the composition.



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference MJL/C155.1/0	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB99/01650	International filing date (day/month/year) 26/05/1999	Priority date (day/month/year) 28/05/1998
International Patent Classification (IPC) or national classification and IPC C07H3/04		
Applicant OXOID LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 5 sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 5 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 25/11/1999	Date of completion of this report 16.08.2000
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Korsner, S-E Telephone No. +49 89 2399 8554 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/01650

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.)*:

Description, pages:

1-34 as originally filed

Claims, No.:

1-34 with telefax of 07/07/2000

Drawings, sheets:

1/8-8/8 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/01650

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-34
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-34
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-34
	No:	Claims	

2. Citations and explanations

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

V. Reasoned statement

The following documents will be referred to in this report:

D1 = Analytical Biochemistry; 1993, pages 49-56

D2 = Carbohydrate Research; 1984, pages 147-163

Novelty (Article 33(2) PCT)

D1, which is referred to on page 3 (top), discloses i.a. peaks that may contain overlapping compounds.

Whether these - in such case - should be considered novelty-destroying will be a matter to settle under later national/regional regulations.

Inventive step (Article 33(3) PCT)

No objection in view of the cited prior art.

VIII. Certain observations

Claims:

1.

Claim 2 has been added in view of D2, which discloses an accidentally overlapping compound 4 (n=3).

Since Claim 2 is dependent on Claim 1, the disclaimer should rather have been added to the independent claim.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/01650

[Whether the differing wordings of these claims, "isolated compound" and "compound", are of importance has to be settled in a later national/regional phase.]

2.

Figure 2 should preferably be included in Claim 1.

3.

The definition "X may be" in Claim 1 is unclear.

4.

Claims 5 and 8 should preferably refer to the compound of Claim 1 in order to avoid repeating the various definitions [subject to national requirements].

5.

Claim 19 has been accepted because of the wording "specific binding".

6.

The Applicant may later have to provide copies of the deposit receipts; see e.g. Rule 28 EPC.

7.

Claims 30-31 and 33 include the step of administering a composition to a mammalian subject.

Such claims may not be acceptable under all national/regional regulations; in case of a later European phase the claims can be redrafted with a view to the Guidelines, C-IV, 4.2.

- - -

CLAIMS

1. An isolated compound having the structure shown in Figure 2, wherein n is an integer between 3 and 10 (inclusive) and X may be H, OH, alkyl, aryl, amyl, or an amino acid residue (optionally substituted) or a sugar residue (optionally substituted), and wherein R and R^1 are hydrophobic hydrocarbon or fatty acid chains (R may be the same as R^1 or different).
2. A compound according to claim 1, where n is an integer other than 3.
3. A compound according to claim 1 or 2, wherein $n = 6$.
4. A compound according to any one of claims 1, 2 or 3, wherein $X = \text{H, OH, D-alanyl or N-acetyl glucosamine.}$
5. A composition, comprising a compound in substantially pure form having the structure shown in Figure 2, wherein n is an integer between 3 and 10 (inclusive) and X is H, OH, alkyl, aryl, amyl, or an amino acid residue (optionally substituted) or a sugar residue (optionally substituted), and R and R^1 are hydrophobic hydrocarbon or fatty acid chains (R may be the same as R^1 , or different).
6. A composition according to claim 5, comprising an isolated compound in accordance with any one of claims 1 to 4.
7. A composition according to claim 5 or 6, in the form of a freeze-dried solid, an aqueous solution, or immobilised on a solid support.
8. A method of testing for a Gram +ve bacterial infection in a mammalian (typically, human) subject, the method comprising the steps of: obtaining a sample of body fluid from the subject; contacting the sample with a composition comprising a compound having the structure shown in Figure 2, wherein n is an integer between 3 and 10 (inclusive) and X is H, OH, alkyl, aryl, amyl, or an amino acid residue (optionally substituted) or a sugar

residue (optionally substituted), and R and R¹ are hydrophobic hydrocarbon or fatty acid chains (R may be the same as R¹, or different); and detecting binding of antibodies (if any) in the sample to the composition.

9. A method according to claim 8, wherein the sample of body fluid obtained from the subject comprises whole blood, serum, urine or saliva.

10. A method according to claim 8 or 9, comprising the detection of binding to the composition of IgG antibodies in the sample.

11. A method according to any one of claims 8, 9 or 10, wherein the test method comprises the performance of an enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), or a Western blot.

12. A method according to any one of claims 8 to 11, for testing for infection caused by Gram +ve cocci.

13. A method according to any one of claims 8 to 12, for testing for infection by a Streptococcus, a Staphylococcus or an Enterococcus.

14. A method according to any one of claims 8 to 13, for diagnosing the presence of a Gram +ve infection associated with a central venous catheter, a cerebrospinal fluid shunt or a prosthetic device.

15. A method according to any one of claims 8 to 14, wherein the composition is in accordance with any one of claims 5-7.

16. A diagnostic test kit for diagnosing the presence of a Gram +ve infection in a mammalian subject, the kit comprising: a solid support for performing a diagnostic test; and a composition in accordance with any one of claims 5-7.

17. A kit according to claim 16, further comprising one or more of the following: labelled

antibody; enzyme substrate; control sample; buffer, and instructions for use.

18. A sterile vaccine composition for use against a Gram +ve infection in a mammalian subject, the vaccine comprising an isolated compound in accordance with any one of claims 1 to 4, or a composition in accordance with any one of claims 5 to 7.

19. An isolated immunoglobulin molecule or variant thereof having specific binding for a compound in accordance with any one of claims 1 to 4.

20. An isolated eukaryotic cell producing an immunoglobulin molecule or variant thereof in accordance with claim 19.

21. A method of making a composition in accordance with any one of claims 5 to 7, the method comprising the steps of: culturing a Gram +ve bacterium in a growth medium so as to cause the bacterium to secrete into the growth medium the compound having the structure shown in Figure 2; separating the growth medium from the bacterial cells; fractionating the growth medium; and isolating that fraction which comprises, in substantially pure form, the compound having the structure shown in Figure 2.

22. *Staphylococcus epidermidis* strain CAN 6KIII, deposited under accession number NCIMB 40896.

23. *Staphylococcus epidermidis* strain HAR 6KIV, deposited under accession number NCIMB 40945.

24. *Staphylococcus epidermidis* strain COS 6KV, deposited under accession number NCIMB 40946.

25. *Staphylococcus epidermidis* strain MIL 6LI, deposited under accession number NCIMB 40947.

26. *Staphylococcus epidermidis* strain HED 6LI, deposited under accession number

NCIMB 40948.

27. *Staphylococcus haemolyticus* strain ONE 6KVI, deposited under accession number NCIMB 40949.

28. *Micrococcus kristinae* strain MAT 6LII, deposited under accession number NCIMB 40950.

29. A method according to claim 21, comprising the step of culturing one or more organisms selected from the group consisting of: *Staphylococcus epidermidis* strain CAN 6KIII; *Staphylococcus epidermidis* strain HAR 6KIV; *Staphylococcus epidermidis* strain COS 6KV; *Staphylococcus epidermidis* strain MIL 6LI; *Staphylococcus epidermidis* strain HED 6LI; *Staphylococcus haemolyticus* strain ONE 6KVI; *Micrococcus kristinae* strain MAT 6LII.

30. A method of making an immunoglobulin having specific binding for a molecule in accordance with claim 1, the method comprising the steps of: preparing a composition comprising a compound in accordance with any one of claims 1-4; administering the composition to a mammalian subject; and obtaining from the subject a sample comprising antibodies or antibody-producing cells.

31. A method according to claim 30, wherein antibody-producing cells are isolated from the subject and used to prepare a hybridoma.

32. A method of obtaining an immunoglobulin or antigen-binding variant thereof having specific binding for a compound in accordance with any one of claims 1-4, the method comprising the steps of: screening a library of viruses or other particles displacing an immunoglobulin or antigen-binding variant thereof on their surface; and selecting those members of the library which display an immunoglobulin or antigen-binding variant thereof which bind to the compound.

33. A method of inducing antibodies in a human subject, the method comprising the steps

of preparing a physiologically acceptable composition in accordance with claim 5; and administering the composition to the subject.

34. A vaccine for inducing antibodies in a mammalian subject the vaccine comprising a composition in accordance with claim 5 and a physiologically acceptable excipient, carrier or diluent.

09/701289 5F00

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
2 December 1999 (02.12.1999)

PCT

(10) International Publication Number
WO 99/61913 A3

(51) International Patent Classification⁶: C07H 3/04,
C07K 1/00, A61K 31/70, C12N 15/06, 1/20, A61K
39/085, C07K 16/12 // (C12N 1/20, C12R 1:45)

West Midlands B74 4NR (GB). ELLIOTT, Thomas, Stuart, Jackson [GB/GB]; 57 Roman Lane, Little Aston Park, Sutton Coldfield, Birmingham B74 3AE (GB).

(21) International Application Number: PCT/GB99/01650

(74) Agent: KEITH W NASH & CO.; 90-92 Regent Street, Cambridge CB2 1DP (GB).

(22) International Filing Date: 26 May 1999 (26.05.1999)

(81) Designated State (*national*): US.

(25) Filing Language: English

(84) Designated States (*regional*): European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

(26) Publication Language: English

(30) Priority Data:

9811347.5

28 May 1998 (28.05.1998) GB

Published:

— With international search report.

(71) Applicant (*for all designated States except US*): OXOID LIMITED [GB/GB]; Kingsland Business Park, Wade Road, Basingstoke, Hampshire RG24 8PW (GB).

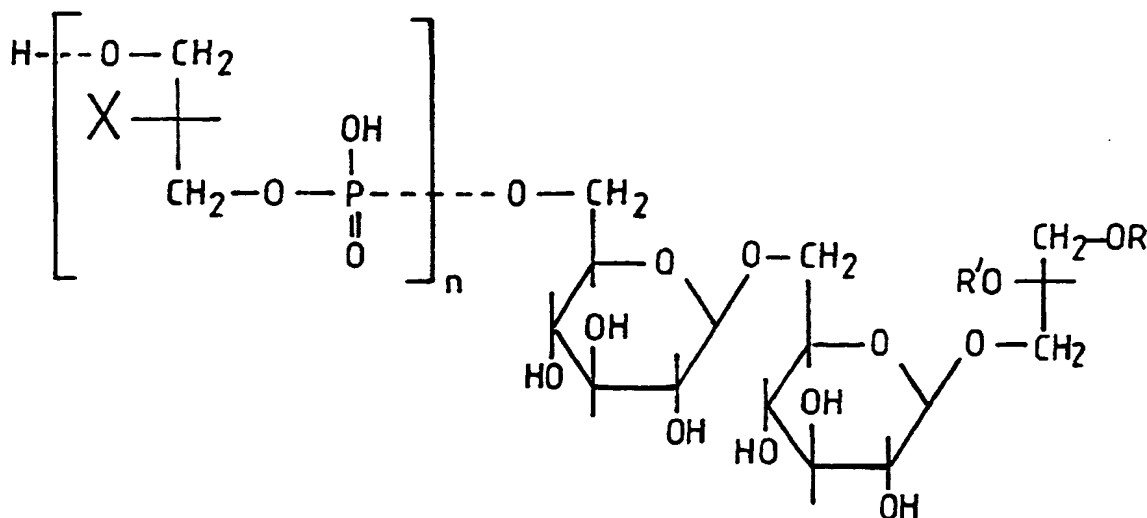
(88) Date of publication of the international search report:
19 April 2001

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): LAMBERT, Peter, Anthony [GB/GB]; 125 Walsall Road, Sutton Coldfield,

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ANTIBACTERIAL DIASCCHARIDE DERIVATIVES



(57) Abstract: Disclosed is an isolated compound having the structure shown in Figure 2, wherein n is an integer between 3 and 10 (inclusive) and X may be H, OH, alkyl, aryl, amyl, or an amino acid residue (optionally substituted) or a sugar residue (optionally substituted), and wherein R and R¹ are hydrophobic hydrocarbon or fatty acid chains (R may be the same as R¹ or different), a method of preparing compositions comprising the compound, and a diagnostic method comprising use of the composition.

WO 99/61913 A3

INTERNATIONAL SEARCH REPORT

al Application No

PCT/GB 99/01650

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07H3/04 C07K1/00 A61K31/70 C12N15/06 C12N1/20
A61K39/085 C07K16/12 //(C12N1/20, C12R1:45)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07H C07K A61K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	J.J.OLTVOORT ET AL.: "Synthesis of a Lipoteichoic Acid-Carrier Fragment of Staphylococcus aureus." CARBOHYDRATE RESEARCH, vol. 130, 1984, pages 147-163, XP002120748 ELSEVIER SCIENTIFIC PUBLISHING COMPANY. AMSTERDAM., NL ISSN: 0008-6215 page 148, compound 4	1,4,7
A	WO 97 42343 A (PHARMACIA AND UPJOHN COMPANY) 13 November 1997 (1997-11-13) the whole document -/-	1,4,7, 15,18-20

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

28 October 1999

Date of mailing of the international search report

11/11/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Scott, J

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	W.FISCHER: "Molecular Analysis of Lipid Macroamphiphiles by Hydrophobic Interaction Chromatography Exemplified with Lipotechoic Acids." ANALYTICAL CHEMISTRY, vol. 208, 1993, pages 49-56, XP002120749 cited in the application abstract	1,4
A	H.I.WERGELAND ET AL.: "Antibodies to Staphylococcal Peptidoglycan and its Peptide Epitopes, Techoic Acid, and Lipotechoic Acid in Sera from Blood Donors and Patients with Staphylococcal Infections." JOURNAL OF CLINICAL MICROBIOLOGY, vol. 27, no. 6, June 1989 (1989-06), pages 1286-1291, XP002120750 cited in the application abstract	1,4
A	J.J.OLTVOORT ET AL.: "A Simple Approach to the Synthesis of a Membrane Techoic Acid Fragment of Staphylococcus aureus." RECUEIL, JOURNAL OF THE ROYAL NETHERLANDS CHEMICAL SOCIETY, vol. 101, no. 3, March 1982 (1982-03), pages 87-91, XP002120751 the whole document	1,4
A	DATABASE WPI Section Ch, Week 198703 Derwent Publications Ltd., London, GB; Class B04, AN 1987-017786 XP002120752 & JP 61 275217 A (YAKULT HONSHA KK), 5 December 1986 (1986-12-05) abstract	1,4

INTERNATIONAL SEARCH REPORT
Information on patent family members

International Application No
PCT/GB 99/01650

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9742343 A	13-11-1997	AU 2746997 A EP 0901529 A WO 9742311 A	26-11-1997 17-03-1999 13-11-1997
JP 61275217 A	05-12-1986	NONE	